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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,006	08/18/2008	Angela Bardotti	PAT051667-US-PCT	6482

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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/21/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/593,006	BARDOTTI ET AL.
	Examiner	Art Unit
	KHATOL SHAHNAN SHAH	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-17 and 19-34* is/are pending in the application.

4a) Of the above claim(s) *16,17 and 19-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-15 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

1. Applicants' amendments after non- final rejection and reply received 3/22/2011 are acknowledged. Claims 1-4, 15-17, 19, 32-34 have been amended.

Status of Claims

2. Claims 1-4, 6-17 and 19-34 are pending. Claims 16, 17, and 19-31 are withdrawn. Claims 1-4, 6-15 and 32-34 are presently under examination. Claims 5 and 18 have been canceled by a previous amendment.

Rejections Withdrawn

3. Rejection of claims 3 and 32-34 under 35 U.S.C. 112, second paragraph, made in paragraph 8 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

4. Rejection of claims 1-3 under 35 U.S.C. 102 (b), made in paragraph 10 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

Rejections Maintained

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Rejection of claims 1-9 and 32-34 under 35 U.S.C. 103(a), made in paragraph 12 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

The rejection was as stated below:

Claims 1-9 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bardotti et al. (Vaccine 18: 1982-1993, 3 April 2000) in view of Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54 September 24, 1999). Prior art of record.

The claims are drawn to a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through a solid phase extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample.

Bardotti et al. teach a method of analyzing a sample's unconjugated saccharide content, comprising the steps of(i) passing the sample through an extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample (see abstract, material, methods and table 1). Bardotti et al. teach a glycoconjugate vaccine (see page 1983) single and combined vaccine (see table 1) measuring total sacchride content (see tables 1 and 2). Bardotti et al. teach quantitative conjugate analysis techniques, such as high performance anion exchange chromatography with pulsed amperometric detection (HPAEC-PAD) see abstract. Bardotti et al. do not teach a solid phase extraction device. However, these devices are well known in the art for example Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54, September 24, 1999) teach solid phase extraction, its method development and sorbents (see abstract).

It would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Bardotti et al. to obtain the instant invention. One of ordinary skilled in the art would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of

organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE (see Hennion pages 4-5).

As to limitations of claims 32-34 such as releasing vaccine for use, packaging and adjusting pH. These are considered optimization of experimental parameters. However, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235(CCPA 1955).

7. Applicants' arguments filed 3/22/2011 have been fully considered but they are not persuasive.

Applicants Argue:

- Turning to the teachings of the references cited by the Examiner, Bardotti *et al.* teaches the separation of unconjugated saccharide from conjugated saccharide through ultrafiltration (one of the available methods discussed above), but does not teach SPE. Hennion teaches general information regarding SPE, but it does not provide any teaching of separating unconjugated capsular saccharide from conjugated capsular saccharide by SPE, or the SPE can be used in a manner that allows such separation without being dependent upon the nature of the capsular saccharide. Thus, an important difference between the art cited by the Examiner and the present claims is that neither of the cited references teach that SPE can advantageously be used for the separation of unconjugated saccharide from conjugated saccharide. To address this deficiency, the Examiner states that it "would have been prima facie obvious to one of ordinary skill in the art at the time of invention to use a solid phase extraction device in the method of Bardotti et al. to obtain the instant invention. One of ordinary skill in the art would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which have encouraged the requirement for solvent free procedures and growth of SPE." Applicants respectfully assert that neither of these reasons are sufficient to establish the

obviousness of the pending claims. According to the MPEP, "[t]he key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious" (MPEP 2142). As indicated above, the Examiner stated that one of ordinary skill would have been motivated to use the SPE teachings of Hennion with the method of Bardotti *et al.* because of SPE's "popularity." The fact that one reference teaches a "popular" technique does not, in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed invention. Instead, the Examiner must articulate a reason to combine the references to arrive at a claimed invention. In this case, the Examiner's citation to "popularity" fails to provide an adequate teaching, suggestion, or motivation that would have led one of ordinary skill in the art to combine Bardotti *et al.* and Hennion to arrive at the claimed invention. Scientists are not lemmings that follow other scientists simply to follow a trend. A scientist would look at the reason why a technique or technology is "popular" to understand whether the reason benefits their particular project or need. The only such underlying reason cited by the Examiner is reduction of "usage of organic solvents in the laboratories." This similarly fails to provide an adequate teaching, suggestion, or motivation that would have led one of ordinary skill in the art to combine Bardotti *et al.* and Hennion to arrive at the claimed invention. A scientist of ordinary skill would have no reason to modify Bardotti *et al.* in view of Hennion to reduce "usage of organic solvents in the laboratories." In Bardotti *et al.,* the method for separating conjugated and unconjugated saccharides uses aqueous, not organic, solvents. In Bardotti *et al.,* unconjugated saccharides are separated from conjugated saccharides through ultrafiltration, using 0.9% NaC1 solution (Bardotti *et al.,* page 1983, left column). In contrast, Hennion frequently provides for the use of organic solvents (e.g. page 13, left column "octanol"; page 15, fight column "acetonitrile", "methanol"; etc.). Thus, modifying Bardotti *et al.* in view of Hennion would actually increase, not decrease, the use of organic solvents.For at least this reason, a person of skill in the art seeking to reduce "usage of organic solvents in the laboratories"

would have no motivation whatsoever to modify Bardotti *et al.* in view of Hennion. Additionally, Applicants respectfully note that Hennion does not provide a teaching of a method for separating unconjugated saccharides from conjugated saccharides, or teach a separation method that does not depend on the nature of the saccharide. A person of skill in the art seeking to improve the method of Bardotti *et al.* would have no reason to modify Bardotti *et al.* in view of Hennion, because Hennion provides no discernable benefit for the separation of unconjugated saccharides from conjugated saccharides over the method Bardotti *et al.*

8. In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Bardotti et al. to obtain the instant invention.

As to applicants' arguments that "the fact that one reference teaches a "popular" technique does not, in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed invention" and reduction of organic solvents . It is this office position that Hennion teaches other advantages of SPE

besides being a popular technique in extraction and separation art. Hennion abstract recites:

"The objective of this review is to provide updated information about the most important features of the new solid-phase extraction (SPE) materials, their interaction mode and then- potential for modem SPE. First, the recent developments are given in formats, phases, *automation,* high throughput purpose and set-up of new types of procedures **Emphasis is then placed on the large choice of sorbents for trapping analytes over a wide range of polarities**, such as highly cross-linked copolymers, functionalized copolymers, graphitized carbons or some specific n-alkylsilicas. The method development is given which is based on prediction from liquid chromatographic retention data or solvation parameters in order can be **to determine the main parameters of any sequence (type and amount of sorbent, sample volume which applied without loss of recovery)**, composition and volume of the clean-up solution, composition and volume of the desorption solution). **Obtaining extracts free from matrix interferences in a few steps one step when possible is now included in the development of SPE procedure**. New selective phases such as mixed-mode and restricted access matrix sorbents or emerging phases such as immunosorbents or molecularly imprinted polymers are reviewed. Selectivity obtained by combining two sorbents is described with the use of ion-exchange or ion-pan sorbents. Special attention is given to **complete automation of the SPE** sequence with its on-line coupling with liquid chromatography followed by various detection modes. This represents a fast, modem and reliable approach to trace analysis."

9. Rejection of claims 1-15 under 35 U.S.C. 103(a), made in paragraph 13 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

The rejection was as stated below:

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei et al. (Dev. Biol (Basel) vol. 103, pp. 259-264, 2000) in view of Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54, September 24, 1999). Prior art of record.

The claims are drawn to a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through a solid phase extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample.

Lei et al. teach a method of analyzing a sample's unconjugated saccharide content, comprising the steps of(i) passing the sample through an extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample (see abstract). Lei et al. teach a glycoconjugate vaccine (see abstract) single and combined vaccine, measuring total sacchride content (see abstract). Lei et al. teach limitations of claims 10-15 meningococcal vaccines prepared from *Neisseria meningitis* serogroups A, C, W 135 and Y (see abstract). Lei et al. teach quantitative conjugate analysis techniques, such as high performance anion exchange chromatography with pulsed amperometric detection (HPAEC-PAD) see abstract. Lei et al. do not teach a solid phase extraction device. However, these devices are well known in the art for example Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54 September 24, 1999) teach solid phase extraction, its method development and sorbents (see abstract).

It would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Lei et al. to obtain the instant invention. One of ordinary skilled in the art would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE (see Hennion pages 4-5).

10. Applicants' arguments filed 3/22/2011 have been fully considered but they are not persuasive.

Applicants Argue:

- In Lei *et al.* as in Bardotti *et al.,* the method for separating conjugated and unconjugated saccharides uses aqueous, not organic, solvents. In Lei *et al.,* unconjugated saccharides are separated from conjugated saccharides by the addition of deoxycholic acid (DOC) to the saccharide sample. Lei *et al.* states that the DOC solution was "prepared first by either dissolving DOC in pH>12 solution or by directly dissolving DOC sodium in salt water" (Lei et al., page 260, middle). In contrast, Hennion frequently provides for the use of organic solvents (e.g. page 13, left column "octanol"; page 15, right column "acetonitrile", "methanol"; etc.). Thus, modifying Lei *et al.* in view of Hennion would actually increase, not decrease, the use of organic solvents. For at least this reason, a person of skill in the art seeking to reduce "usage of organic solvents in the laboratories" would have no motivation whatsoever to modify Lei *et al.* in view of Hennion. Additionally, as noted above, Applicants respectfully note that Hennion does not provide a teaching of a method for separating unconjugated saccharides from conjugated saccharides, or teach a separation method that does not depend on the nature of the saccharide. A person of skill in the art seeking to improve the method of Lei *et al.* would have no reason to modify Lei *et al.* in view of Hennion, because Hennion provides no discernable benefit for the separation of unconjugated saccharides from conjugated saccharides over the method Lei *et al.* For at least these reasons, the Examiner has failed to establish the obviousness of the pending claims over Lei *et al.* in view of Hennion.

11. In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the

claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Lei et al. to obtain the instant invention.

As to applicants' arguments that "the fact that one reference teaches a "popular" technique does not, in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed invention" and reduction of organic solvents. It is this office position that Hennion teaches other advantages of SPE besides being a popular technique in extraction and separation art. Hennion abstract recites:

"The objective of this review is to provide updated information about the most important features of the new solid-phase extraction (SPE) materials, their interaction mode and then- potential for modem SPE. First, the recent developments are given in formats, phases, *automation,* high throughput purpose and set-up of new types of procedures **Emphasis is then placed on the large choice of sorbents for trapping analytes over a wide range of polarities**, such as highly cross-linked copolymers, functionalized copolymers, graphitized carbons or some specific n-alkylsilicas. The method development is given which is based on prediction from liquid chromatographic retention data or solvation parameters in order can be **to determine the main parameters of any sequence (type and amount of sorbent, sample volume which applied without loss of recovery)**, composition and volume of the clean-up solution, composition and volume of the desorption solution). **Obtaining extracts free from matrix interferences in a few steps one step when possible is now included in the development of SPE procedure**. New selective phases such as mixed-mode and restricted access matrix sorbents or emerging phases such as

immunosorbents or molecularly imprinted polymers are reviewed. Selectivity obtained by combining two sorbents is described with the use of ion-exchange or ion-pan sorbents. Special attention is given to **complete automation of the SPE** sequence with its on-line coupling with liquid chromatography followed by various detection modes. This represents a fast, modem and reliable approach to trace analysis."

Conclusion

12. No claims are allowed.

13. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KHATOL SHAHNAN SHAH whose telephone number is (571)272-0863. The examiner can normally be reached on Mon, Wed 12:30-6:30 pm, Thurs-Fri 12:30-4:30pm pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571)-272 0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Khatol S Shahnan-Shah/
Examiner, Art Unit 1645
June 17, 2011

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1645